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EXAMINER

CANELLA, KAREN A

ART UNIT PAPER NUMBER

1642

DATE MAILED: 07/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/738,625

Applicant(s)

GLAZIER, ARNOLD

Examiner

Karen A Canella

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☐ Claim(s) ____ is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☒ Claim(s) 1-29 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

DETAILED ACTION

1. Claims 1-29 are pending.

Election/Restrictions

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:
 - I. Claims 1-29, drawn to an anticancer drug or a set of anticancer drugs, wherein the anticancer drug or the set of anticancer drugs comprises tumor selective targeting ligands which differ from each other within the drug or and within the set of drugs and methods of treating cancer comprising the administration of said drugs, wherein one of the tumor selective targeting ligands binds to a first target receptor which is a cathepsin protease, cathepsin B, cathepsin D, cathepsin K, cathepsin L or cathepsin O, classified, for example, in class 424, subclasses 130.1 and 178.1, and class 514, subclass 2.
 - II. Claims 1-29, drawn to an anticancer drug or a set of anticancer drugs, wherein the anticancer drug or the set of anticancer drugs comprises tumor selective targeting ligands which differ from each other within the drug or and within the set of drugs and methods of treating cancer comprising the administration of said drugs, wherein one of the tumor selective targeting ligands binds to a first target receptor which is a collagenase, a gelatinase, or stromelysin 3, classified, for example, in class 424, subclasses 130.1 and 178.1, and class 514, subclass 2..
 - III. Claims 1-29, drawn to an anticancer drug or a set of anticancer drugs, wherein the anticancer drug or the set of anticancer drugs comprises tumor selective targeting ligands which differ from each other within the drug or and within the set of drugs and methods of treating cancer comprising the administration of said drugs, wherein one of the tumor selective targeting ligands binds to a first target receptor which is a matrix metalloproteinase receptor, a membrane type matrix metalloproteinase receptor, receptors for MMP1, MMP2, MMP3, MMP7, MMP9, MMP12, and MMP13, a membrane-type matrix metalloproteinase I receptor, matrilysin receptor or

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a matripase receptor, classified, for example, in class 424, subclasses 130.1 and 178.1, and class 514, subclass 2.. Matripase is placed with this group to the extent that it is a matrix metalloproteinase. A brief search of the literature indicates that the term "matripase" is not recognized in the art.

- IV. Claims 1-29, drawn to an anticancer drug or a set of anticancer drugs, wherein the anticancer drug or the set of anticancer drugs comprises tumor selective targeting ligands which differ from each other within the drug or and within the set of drugs and methods of treating cancer comprising the administration of said drugs, wherein one of the tumor selective targeting ligands binds to a first target receptor which is an alpha V beta 3 integrin or a laminin receptor, classified, for example, in class 424, subclasses 130.1 and 178.1, and class 514, subclass 2.
- V. Claims 1-29, drawn to an anticancer drug or a set of anticancer drugs, wherein the anticancer drug or the set of anticancer drugs comprises tumor selective targeting ligands which differ from each other within the drug or and within the set of drugs and methods of treating cancer comprising the administration of said drugs, wherein one of the tumor selective targeting ligands binds to a first target receptor which is a bombesin/gastrin releasing peptide receptor, a gastrin/cholecystokinin type B receptor, or a somatostatin receptor, classified, for example, in class 424, subclasses 130.1 and 178.1, and class 514, subclass 2.
- VI. Claims 1-29, drawn to an anticancer drug or a set of anticancer drugs, wherein the anticancer drug or the set of anticancer drugs comprises tumor selective targeting ligands which differ from each other within the drug or and within the set of drugs and methods of treating cancer comprising the administration of said drugs, wherein one of the tumor selective targeting ligands binds to a first target receptor which is a fibroblast activation protein receptor, classified, for example, in class 424, subclasses 130.1 and 178.1, and class 514, subclass 2.

- VII. Claims 1-29, drawn to an anticancer drug or a set of anticancer drugs, wherein the anticancer drug or the set of anticancer drugs comprises tumor selective targeting ligands which differ from each other within the drug or and within the set of drugs and methods of treating cancer comprising the administration of said drugs, wherein one of the tumor selective targeting ligands binds to a first target receptor which is a folate binding receptor, classified, for example, in class 424, subclasses 130.1 and 178.1, and class 514, subclass 2.
- VIII. Claims 1-29, drawn to an anticancer drug or a set of anticancer drugs, wherein the anticancer drug or the set of anticancer drugs comprises tumor selective targeting ligands which differ from each other within the drug or and within the set of drugs and methods of treating cancer comprising the administration of said drugs, wherein one of the tumor selective targeting ligands binds to a first target receptor which is a plasmin or urokinase receptor, classified, for example, in class 424, subclasses 130.1 and 178.1, and class 514, subclass 2.
- IX. Claims 1-29, drawn to an anticancer drug or a set of anticancer drugs, wherein the anticancer drug or the set of anticancer drugs comprises tumor selective targeting ligands which differ from each other within the drug or and within the set of drugs and methods of treating cancer comprising the administration of said drugs, wherein one of the tumor selective targeting ligands binds to a first target receptor which is a melanocyte stimulating hormone receptor, classified, for example, in class 424, subclasses 130.1 and 178.1, and class 514, subclass 2.
- X. Claims 1-29, drawn to an anticancer drug or a set of anticancer drugs, wherein the anticancer drug or the set of anticancer drugs comprises tumor selective targeting ligands which differ from each other within the drug or and within the set of drugs and methods of treating cancer comprising the administration of said drugs, wherein one of the tumor selective targeting ligands binds to a first target receptor which is a sigma receptor, classified,

for example, in class 424, subclasses 130.1 and 178.1, and class 514, subclass 2.

- XI. Claims 1-29, drawn to an anticancer drug or a set of anticancer drugs, wherein the anticancer drug or the set of anticancer drugs comprises tumor selective targeting ligands which differ from each other within the drug or and within the set of drugs and methods of treating cancer comprising the administration of said drugs, wherein one of the tumor selective targeting ligands binds to a first target receptor which is a seprase receptor or a trypsin receptor, classified, for example, in class 424, subclasses 130.1 and 178.1, and class 514, subclass 2.
- XII. Claims 1-29, drawn to an anticancer drug or a set of anticancer drugs, wherein the anticancer drug or the set of anticancer drugs comprises tumor selective targeting ligands which differ from each other within the drug or and within the set of drugs and methods of treating cancer comprising the administration of said drugs, wherein one of the tumor selective targeting ligands binds to a first target receptor which is a nitrobenzylthioinosine-binding receptors or nucleoside transporter proteins, classified, for example, in class 424, subclasses 130.1 and 178.1, and class 514, subclass 2.
- XIII. Claims 1-29, drawn to an anticancer drug or a set of anticancer drugs, wherein the anticancer drug or the set of anticancer drugs comprises tumor selective targeting ligands which differ from each other within the drug or and within the set of drugs and methods of treating cancer comprising the administration of said drugs, wherein one of the tumor selective targeting ligands binds to a first target receptor which is norepinephrine transporters or peripheral benzodiazepan binding receptors, classified, for example, in class 424, subclasses 130.1 and 178.1, and class 514, subclass 2.
- XIV. Claims 1-29, drawn to an anticancer drug or a set of anticancer drugs, wherein the anticancer drug or the set of anticancer drugs comprises tumor selective targeting ligands which differ from each other within the drug or

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and within the set of drugs and methods of treating cancer comprising the administration of said drugs, wherein one of the tumor selective targeting ligands binds to a first target receptor which is glutamate carboxypeptidase II, classified, for example, in class 424, subclasses 130.1 and 178.1, and class 514, subclass 2.

- XV. Claims 1-29, drawn to an anticancer drug or a set of anticancer drugs, wherein the anticancer drug or the set of anticancer drugs comprises tumor selective targeting ligands which differ from each other within the drug or and within the set of drugs and methods of treating cancer comprising the administration of said drugs, wherein one of the tumor selective targeting ligands binds to a first target receptor which is guanidinobenzoate, classified, for example, in class 424, subclasses 130.1 and 178.1, and class 514, subclass 2.

3. In the event that applicant elects group I, a further restriction will apply to targeting ligands that bind to the second target receptor which are selected from the group consisting of

- A. a collagenase, a gelatinase, or stromelysin 3,
- B. a matrix metalloproteinase receptor, a membrane type matrix metalloproteinase receptor, receptors for MMP1, MMP2, MMP3, MMP7, MMP9, MMP12, and MMP13, a membrane-type matrix metalloproteinase I receptor, matrilysin receptor or a matrilysin receptor,
- C. an alpha V beta 3 integrin or a laminin receptor,
- D. a bombesin/gastrin releasing peptide receptor, a gastrin/cholecystokinin type B receptor, or a somatostatin receptor,
- E. a fibroblast activation protein receptor,
- F. a folate binding receptor,
- G. a plasmin or urokinase receptor,
- H. a melanocyte stimulating hormone receptor
- I. a sigma receptor

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- J. a seprase receptor or a trypsin receptor
- K. a nitrobenzylthioinosine-binding receptors or nucleoside transporter proteins,
- L. norepinephrine transporters or peripheral benzodiazepan binding receptors,
- M. glutamate carboxypeptidase II, and
- N. guanidinobenzoatase.

Applicant is required to selected a group from A-N for examination as the second target receptor wherein the first target receptor is defined in invention I. Please note that this is a further restriction requirement, not an election of species.

4. In the event that applicant elects group II, a further restriction will apply to targeting ligands that bind to the second target receptor which are selected from the group consisting of

- A. a cathepsin protease, cathepsin B, cathepsin D, cathepsin K, cathepsin L or cathepsin O,
- B. a matrix metalloproteinase receptor, a membrane type matrix metalloproteinase receptor, receptors for MMP1, MMP2, MMP3, MMP7, MMP9, MMP12, and MMP13, a membrane-type matrix metalloproteinase I receptor, matrilysin receptor or a matripase receptor,
- C. an alpha V beta 3 integrin or a laminin receptor,
- D. a bombesin/gastrin releasing peptide receptor, a gastrin/cholecystokinin type B receptor, or a somatostatin receptor,
- E. a fibroblast activation protein receptor,
- F. a folate binding receptor,
- G. a plasmin or urokinase receptor,
- H. a melanocyte stimulating hormone receptor
- I. a sigma receptor
- J. a seprase receptor or a trypsin receptor

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K. a nitrobenzylthioinosine-binding receptors or nucleoside transporter proteins,

L. norepinephrine transporters or peripheral benzodiazepan binding receptors,

M. glutamate carboxypeptidase II, and

N. guanidinobenzoate.

Applicant is required to selected a group from A-N for examination as the second target receptor wherein the first target receptor is defined in invention II. Please note that this is a further restriction requirement, not an election of species.

5. In the event that applicant elects group III a further restriction will apply to targeting ligands that bind to the second target receptor which are selected from the group consisting of

A. a cathepsin protease, cathepsin B, cathepsin D, cathepsin K, cathepsin L or cathepsin O,

B. a collagenase, a gelatinase, or stromelysin 3r,

C. an alpha V beta 3 integrin or a laminin receptor,

D. a bombesin/gastrin releasing peptide receptor, a gastrin/cholecystokinin type B receptor, or a somatostatin receptor,

E. a fibroblast activation protein receptor,

F. a folate binding receptor,

G. a plasmin or urokinase receptor,

H. a melanocyte stimulating hormone receptor

I. a sigma receptor

J. a seprase receptor or a trypsin receptor

K. a nitrobenzylthioinosine-binding receptors or nucleoside transporter proteins,

L. norepinephrine transporters or peripheral benzodiazepan binding receptors,

M. glutamate carboxypeptidase II, and

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N. guanidinobenzoatase.

Applicant is required to select a group from A-N for examination as the second target receptor wherein the first target receptor is defined in invention III. Please note that this is a further restriction requirement, not an election of species.

6. In the event that applicant elects group IV a further restriction will apply to targeting ligands that bind to the second target receptor which are selected from the group consisting of

- A. a cathepsin protease, cathepsin B, cathepsin D, cathepsin K, cathepsin L or cathepsin O,
- B. a collagenase, a gelatinase, or stromelysin 3r,
- C. a matrix metalloproteinase receptor, a membrane type matrix metalloproteinase receptor, receptors for MMP1, MMP2, MMP3, MMP7, MMP9, MMP12, and MMP13, a membrane-type matrix metalloproteinase I receptor, matrilysin receptor or a matrilysin receptor,
- D. a bombesin/gastrin releasing peptide receptor, a gastrin/cholecystokinin type B receptor, or a somatostatin receptor,
- E. a fibroblast activation protein receptor,
- F. a folate binding receptor,
- G. a plasmin or urokinase receptor,
- H. a melanocyte stimulating hormone receptor
- I. a sigma receptor
- J. a seprase receptor or a trypsin receptor
- K. a nitrobenzylthioinosine-binding receptors or nucleoside transporter proteins,
- L. norepinephrine transporters or peripheral benzodiazepan binding receptors,
- M. glutamate carboxypeptidase II, and
- N. guanidinobenzoatase.

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Applicant is required to select a group from A-N for examination as the second target receptor wherein the first target receptor is defined in invention IV. Please note that this is a further restriction requirement, not an election of species.

7. In the event that applicant elects group V a further restriction will apply to targeting ligands that bind to the second target receptor which are selected from the group consisting of

- A. a cathepsin protease, cathepsin B, cathepsin D, cathepsin K, cathepsin L or cathepsin O,
- B. a collagenase, a gelatinase, or stromelysin 3r,
- C. a matrix metalloproteinase receptor, a membrane type matrix metalloproteinase receptor, receptors for MMP1, MMP2, MMP3, MMP7, MMP9, MMP12, and MMP13, a membrane-type matrix metalloproteinase I receptor, matrilysin receptor or a matrilysin receptor,
- D. an alpha V beta 3 integrin or a laminin receptor,
- E. a fibroblast activation protein receptor,
- F. a folate binding receptor,
- G. a plasmin or urokinase receptor,
- H. a melanocyte stimulating hormone receptor
- I. a sigma receptor
- J. a seprase receptor or a trypsin receptor
- K. a nitrobenzylthioinosine-binding receptors or nucleoside transporter proteins,
- L. norepinephrine transporters or peripheral benzodiazepan binding receptors,
- M. glutamate carboxypeptidase II, and
- N. guanidinobenzoate.

Applicant is required to select a group from A-N for examination as the second target receptor wherein the first target receptor is defined in invention V. Please note that this is a further restriction requirement, not an election of species.

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8. In the event that applicant elects group VI a further restriction will apply to targeting ligands that bind to the second target receptor which are selected from the group consisting of

- A. a cathepsin protease, cathepsin B, cathepsin D, cathepsin K, cathepsin L or cathepsin O,
- B. a collagenase, a gelatinase, or stromelysin 3r,
- C. a matrix metalloproteinase receptor, a membrane type matrix metalloproteinase receptor, receptors for MMP1, MMP2, MMP3, MMP7, MMP9, MMP12, and MMP13, a membrane-type matrix metalloproteinase I receptor, matrilysin receptor or a matrilysin receptor,
- D. an alpha V beta 3 integrin or a laminin receptor,
- E. a bombesin/gastrin releasing peptide receptor, a gastrin/cholecystokinin type B receptor, or a somatostatin receptor,
- F. a folate binding receptor,
- G. a plasmin or urokinase receptor,
- H. a melanocyte stimulating hormone receptor
- I. a sigma receptor
- J. a seprase receptor or a trypsin receptor
- K. a nitrobenzylthioinosine-binding receptors or nucleoside transporter proteins,
- L. norepinephrine transporters or peripheral benzodiazepan binding receptors,
- M. glutamate carboxypeptidase II, and
- N. guanidinobenzoate.

Applicant is required to select a group from A-N for examination as the second target receptor wherein the first target receptor is defined in invention VI. Please note that this is a further restriction requirement, not an election of species.

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9. In the event that applicant elects group VII a further restriction will apply to targeting ligands that bind to the second target receptor which are selected from the group consisting of

- A. a cathepsin protease, cathepsin B, cathepsin D, cathepsin K, cathepsin L or cathepsin O,
- B. a collagenase, a gelatinase, or stromelysin 3r,
- C. a matrix metalloproteinase receptor, a membrane type matrix metalloproteinase receptor, receptors for MMP1, MMP2, MMP3, MMP7, MMP9, MMP12, and MMP13, a membrane-type matrix metalloproteinase I receptor, matrilysin receptor or a matripase receptor,
- D. an alpha V beta 3 integrin or a laminin receptor,
- E. a bombesin/gastrin releasing peptide receptor, a gastrin/cholecystokinin type B receptor, or a somatostatin receptor,
- F. a fibroblast activation protein receptor,,
- G. a plasmin or urokinase receptor,
- H. a melanocyte stimulating hormone receptor
- I. a sigma receptor
- J. a seprase receptor or a trypsin receptor
- K. a nitrobenzylthioinosine-binding receptors or nucleoside transporter proteins,
- L. norepinephrine transporters or peripheral benzodiazepan binding receptors,
- M. glutamate carboxypeptidase II, and
- N. guanidinobenzoatase.

Applicant is required to selected a group from A-N for examination as the second target receptor wherein the first target receptor is defined in invention VII. Please note that this is a further restriction requirement, not an election of species.

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10. In the event that applicant elects group VIII a further restriction will apply to targeting ligands that bind to the second target receptor which are selected from the group consisting of

- A. a cathepsin protease, cathepsin B, cathepsin D, cathepsin K, cathepsin L or cathepsin O,
- B. a collagenase, a gelatinase, or stromelysin 3r,
- C. a matrix metalloproteinase receptor, a membrane type matrix metalloproteinase receptor, receptors for MMP1, MMP2, MMP3, MMP7, MMP9, MMP12, and MMP13, a membrane-type matrix metalloproteinase I receptor, matrilysin receptor or a matripase receptor,
- D. an alpha V beta 3 integrin or a laminin receptor,
- E. a bombesin/gastrin releasing peptide receptor, a gastrin/cholecystokinin type B receptor, or a somatostatin receptor,
- F. a fibroblast activation protein receptor,,
- G. a folate binding receptor,
- H. a melanocyte stimulating hormone receptor
- I. a sigma receptor
- J. a seprase receptor or a trypsin receptor
- K. a nitrobenzylthioinosine-binding receptors or nucleoside transporter proteins,
- L. norepinephrine transporters or peripheral benzodiazepan binding receptors,
- M. glutamate carboxypeptidase II, and
- N. guanidinobenzoatase.

Applicant is required to selected a group from A-N for examination as the second target receptor wherein the first target receptor is defined in invention VIII. Please note that this is a further restriction requirement, not an election of species.

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11. In the event that applicant elects group IX a further restriction will apply to targeting ligands that bind to the second target receptor which are selected from the group consisting of

- A. a cathepsin protease, cathepsin B, cathepsin D, cathepsin K, cathepsin L or cathepsin O,
- B. a collagenase, a gelatinase, or stromelysin 3r,
- C. a matrix metalloproteinase receptor, a membrane type matrix metalloproteinase receptor, receptors for MMP1, MMP2, MMP3, MMP7, MMP9, MMP12, and MMP13, a membrane-type matrix metalloproteinase I receptor, matrilysin receptor or a matripase receptor,
- D. an alpha V beta 3 integrin or a laminin receptor,
- E. a bombesin/gastrin releasing peptide receptor, a gastrin/cholecystokinin type B receptor, or a somatostatin receptor,
- F. a fibroblast activation protein receptor,,
- G. a folate binding receptor,
- H. a plasmin or urokinase receptor,
- I. a sigma receptor
- J. a seprase receptor or a trypsin receptor
- K. a nitrobenzylthioinosine-binding receptors or nucleoside transporter proteins,
- L. norepinephrine transporters or peripheral benzodiazepan binding receptors,
- M. glutamate carboxypeptidase II, and
- N. guanidinobenzoatase.

Applicant is required to selected a group from A-N for examination as the second target receptor wherein the first target receptor is defined in invention IX. Please note that this is a further restriction requirement, not an election of species.

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12. In the event that applicant elects group X a further restriction will apply to targeting ligands that bind to the second target receptor which are selected from the group consisting of

- A. a cathepsin protease, cathepsin B, cathepsin D, cathepsin K, cathepsin L or cathepsin O,
- B. a collagenase, a gelatinase, or stromelysin 3r,
- C. a matrix metalloproteinase receptor, a membrane type matrix metalloproteinase receptor, receptors for MMP1, MMP2, MMP3, MMP7, MMP9, MMP12, and MMP13, a membrane-type matrix metalloproteinase I receptor, matrilysin receptor or a matripase receptor,
- D. an alpha V beta 3 integrin or a laminin receptor,
- E. a bombesin/gastrin releasing peptide receptor, a gastrin/cholecystokinin type B receptor, or a somatostatin receptor,
- F. a fibroblast activation protein receptor,,
- G. a folate binding receptor,
- H. a plasmin or urokinase receptor,
- I. a melanocyte stimulating hormone receptor
- J. a seprase receptor or a trypsin receptor
- K. a nitrobenzylthioinosine-binding receptors or nucleoside transporter proteins,
- L. norepinephrine transporters or peripheral benzodiazepan binding receptors,
- M. glutamate carboxypeptidase II, and
- N. guanidinobenzoatase.

Applicant is required to selected a group from A-N for examination as the second target receptor wherein the first target receptor is defined in invention X. Please note that this is a further restriction requirement, not an election of species.

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13. In the event that applicant elects group XI a further restriction will apply to targeting ligands that bind to the second target receptor which are selected from the group consisting of

- A. a cathepsin protease, cathepsin B, cathepsin D, cathepsin K, cathepsin L or cathepsin O,
- B. a collagenase, a gelatinase, or stromelysin 3r,
- C. a matrix metalloproteinase receptor, a membrane type matrix metalloproteinase receptor, receptors for MMP1, MMP2, MMP3, MMP7, MMP9, MMP12, and MMP13, a membrane-type matrix metalloproteinase I receptor, matrilysin receptor or a matripase receptor,
- D. an alpha V beta 3 integrin or a laminin receptor,
- E. a bombesin/gastrin releasing peptide receptor, a gastrin/cholecystokinin type B receptor, or a somatostatin receptor,
- F. a fibroblast activation protein receptor,,
- G. a folate binding receptor,
- H. a plasmin or urokinase receptor,
- I. a melanocyte stimulating hormone receptor
- J. a sigma receptor
- K. a nitrobenzylthioinosine-binding receptors or nucleoside transporter proteins,
- L. norepinephrine transporters or peripheral benzodiazepan binding receptors,
- M. glutamate carboxypeptidase II, and
- N. guanidinobenzoatase.

Applicant is required to selected a group from A-N for examination as the second target receptor wherein the first target receptor is defined in invention XI. Please note that this is a further restriction requirement, not an election of species.

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14. In the event that applicant elects group XII a further restriction will apply to targeting ligands that bind to the second target receptor which are selected from the group consisting of

- A. a cathepsin protease, cathepsin B, cathepsin D, cathepsin K, cathepsin L or cathepsin O,
- B. a collagenase, a gelatinase, or stromelysin 3r,
- C. a matrix metalloproteinase receptor, a membrane type matrix metalloproteinase receptor, receptors for MMP1, MMP2, MMP3, MMP7, MMP9, MMP12, and MMP13, a membrane-type matrix metalloproteinase I receptor, matrilysin receptor or a matripase receptor,
- D. an alpha V beta 3 integrin or a laminin receptor,
- E. a bombesin/gastrin releasing peptide receptor, a gastrin/cholecystokinin type B receptor, or a somatostatin receptor,
- F. a fibroblast activation protein receptor,,
- G. a folate binding receptor,
- H. a plasmin or urokinase receptor,
- I. a melanocyte stimulating hormone receptor
- J. a sigma receptor
- K. a seprase receptor or a trypsin receptor,
- L. norepinephrine transporters or peripheral benzodiazepan binding receptors,
- M. glutamate carboxypeptidase II, and
- N. guanidinobenzoatase.

Applicant is required to selected a group from A-N for examination as the second target receptor wherein the first target receptor is defined in invention XII. Please note that this is a further restriction requirement, not an election of species.

15. In the event that applicant elects group XIII a further restriction will apply to targeting ligands that bind to the second target receptor which are selected from the group consisting of

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- A. a cathepsin protease, cathepsin B, cathepsin D, cathepsin K, cathepsin L or cathepsin O,
- B. a collagenase, a gelatinase, or stromelysin 3r,
- C. a matrix metalloproteinase receptor, a membrane type matrix metalloproteinase receptor, receptors for MMP1, MMP2, MMP3, MMP7, MMP9, MMP12, and MMP13, a membrane-type matrix metalloproteinase I receptor, matrilysin receptor or a matripase receptor,
- D. an alpha V beta 3 integrin or a laminin receptor,
- E. a bombesin/gastrin releasing peptide receptor, a gastrin/cholecystokinin type B receptor, or a somatostatin receptor,
- F. a fibroblast activation protein receptor,,
- G. a folate binding receptor,
- H. a plasmin or urokinase receptor,
- I. a melanocyte stimulating hormone receptor
- J. a sigma receptor
- K. a seprase receptor or a trypsin receptor,
- L. a nitrobenzylthioinosine-binding receptors or nucleoside transporter proteins,
- M. glutamate carboxypeptidase II, and
- N. guanidinobenzoate.

Applicant is required to selected a group from A-N for examination as the second target receptor wherein the first target receptor is defined in invention XIII. Please note that this is a further restriction requirement, not an election of species.

16. In the event that applicant elects group XIV a further restriction will apply to targeting ligands that bind to the second target receptor which are selected from the group consisting of

- A. a cathepsin protease, cathepsin B, cathepsin D, cathepsin K, cathepsin L or cathepsin O,
- B. a collagenase, a gelatinase, or stromelysin 3r,

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- C. a matrix metalloproteinase receptor, a membrane type matrix metalloproteinase receptor, receptors for MMP1, MMP2, MMP3, MMP7, MMP9, MMP12, and MMP13, a membrane-type matrix metalloproteinase I receptor, matrilysin receptor or a matripase receptor,
- D. an alpha V beta 3 integrin or a laminin receptor,
- E. a bombesin/gastrin releasing peptide receptor, a gastrin/cholecystokinin type B receptor, or a somatostatin receptor,
- F. a fibroblast activation protein receptor,,
- G. a folate binding receptor,
- H. a plasmin or urokinase receptor,
- I. a melanocyte stimulating hormone receptor
- J. a sigma receptor
- K. a seprase receptor or a trypsin receptor,
- L. a nitrobenzylthioinosine-binding receptors or nucleoside transporter proteins,
- M. norepinephrine transporters or peripheral benzodiazepan binding receptors, and
- N. guanidinobenzoatase.

Applicant is required to selected a group from A-N for examination as the second target receptor wherein the first target receptor is defined in invention XIV. Please note that this is a further restriction requirement, not an election of species.

17. In the event that applicant elects group XV a further restriction will apply to targeting ligands that bind to the second target receptor which are selected from the group consisting of

- A. a cathepsin protease, cathepsin B, cathepsin D, cathepsin K, cathepsin L or cathepsin O,
- B. a collagenase, a gelatinase, or stromelysin 3r,
- C. a matrix metalloproteinase receptor, a membrane type matrix metalloproteinase receptor, receptors for MMP1, MMP2, MMP3, MMP7,

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MMP9, MMP12, and MMP13, a membrane-type matrix metalloproteinase
I receptor, matrilysin receptor or a matripase receptor,
D. an alpha V beta 3 integrin or a laminin receptor,
E. a bombesin/gastrin releasing peptide receptor, a gastrin/cholecystokinin
type B receptor, or a somatostatin receptor,
F. a fibroblast activation protein receptor,,
G. a folate binding receptor,
H. a plasmin or urokinase receptor,
I. a melanocyte stimulating hormone receptor
J. a sigma receptor
K. a seprase receptor or a trypsin receptor,
L. a nitrobenzylthioinosine-binding receptors or nucleoside transporter
proteins,
M. norepinephrine transporters or peripheral benzodiazepan binding
receptors, and
N. glutamate carboxypeptidase II..

Applicant is required to selected a group from A-N for examination as the second target receptor wherein the first target receptor is defined in invention XV. Please note that this is a further restriction requirement, not an election of species.

18. The inventions are distinct, each from the other because of the following reasons:

Inventions of Groups I through XV are structurally and functionally different products which are made by different methods and have different uses. The examination of all groups would require different searches in the U.S. Patent Shoes and the scientific literature and would require the consideration of different patentability issues.

The methods of Groups I through XV differ in the products used to attain the method objective, wherein said products are made by different methods and have different uses.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their recognized divergent subject matter

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and because the searches required for the groups are not co-extensive, restriction for examination purposes as indicated is proper.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A Canella whose telephone number is (571)292-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571)292-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.

7/8/2004

Karen A. Canella
KARENA CANELLA PH.D
PRIMARY EXAMINER